

**Medicinal Chemistry (MDCH) 5210**  
**Organic Medicinal Chemistry I**  
**Fall Semester 2002, Second Professional Year**  
**10:45-11:40 MW, Skaggs Hall 316**

*Exam 2 (14 October 2002) Study Guide:*

**The exam is at 8:00am (1 hour) in Skaggs Auditorium**

Comments, help, concerns?

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Helpful readings:

- (1) Class notes!
- (2) <http://www.chpc.utah.edu/~cheatham/courses.html>
- (3) Foye; Principles of Medicinal Chemistry
  - a. Chapter 15, Hypnotics
  - b. Chapter 16, [section on Benzodiazepines]
  - c. Chapter 17, [anxiolytic agents]
  - d. Chapter 20 Antiparkinsons agents
- (4) Goodman and Gilman; The Pharmacological Basis of Therapeutics  
[sedative/hypnotics, antiparkinsons agents, ...]

Exam #2 will cover material from the 2<sup>nd</sup> part of the course up through class on Weds 9 October. It will ALSO cover basic principles; it would be wise to review key basic principles such as  $pK_a$ , electron donating/withdrawing groups, *bioisosteres*, ...

- Basic principles + receptors (2 lectures)
- Sedative/Hypnotics (2 lectures)
- Anxiolytics (1.5 lectures)
- Anti-Parkinsons (1 lecture)
- Grapefruit Juice interactions

Emphasis will be on basic principles, common/obvious structure-activity relationships, MOA (mechanism of action) where known, and well-known, well used, and important drugs in each class. We may also test on basic principles (solubility, hydrogen bonding, mechanisms of drug action—physical, receptor binding, ...)

***NOTE: this study guide is not inclusive and is only intended as a guide; in addition to using this guide, please look over the notes... Well known and Top200 drugs are worthwhile to recognize (and name).***

### Basic principles (review again):

- (1) What are the main determinants of water solubility?
- (2) What is polarity / hydrophobicity / hydrophilicity / lipophilicity
- (3) How might we increase or decrease the lifetime (duration) of a given drug?  
[Think about bioavailability *and* metabolism *and* distribution *and* absorption]
- (4) What groups are normally charged or ionizable? What are groups are lipophilic?  
What groups are polar? What groups are electron donating or electron withdrawing?
- (5) **What are bioisosteres?** Know the common bioisosteric substitutions possible for various groups (i.e. ring equivalents, tetravalent substitutions, ...)
- (6) What is  $pK_a$ ? Where are basic/acidic oral drugs absorbed?
- (7) What is an agonist, indirect agonist, competitive antagonist, non-competitive antagonist? **What is an inverse agonist?**

### Sedative/Hypnotics

- (1) Know about the progression of effects of sedative/hypnotics with dose. Some hypnotics are safer than others, why? What is the difference between a sedative and a hypnotic?
- (2) What are EEG, EOG and EMG's? What is REM and NREM sleep?
- (3) Know the structure of  $\gamma$ -aminobutyric acid or GABA. What is GABA? Where does it act?
- (4) Review basic concepts in neurotransmission
- (5) How do alcohol's act as sedative/hypnotics? What are classic examples of alcohols with these properties (that may be used as drugs).

### Barbiturates:

- (1) Know the structure of barbituric acid. Why is this not an effective sedative/hypnotic? [hint: this is not due to toxicity]. How can we modify it to make it better?
- (2) Know the basic SAR of the barbiturates. Why are barbiturates not recommended for use as sleeping pills? What significant side effects (at least four significant ones were discussed)?
- (3) Why do some (highly lipophilic) barbiturates, like Penothal ®, have a short onset and short duration of action?

(4) Know about the various subunits of the GABA receptor and various possible binding sites for agonist/antagonist activity. Remember about the picrotoxin and barbiturate site, where GABA antagonists like bicuculline bind, and where the benzodiazepines bind...

(5) Phenobarbital, mephobarbital, thiopental, ...

(6) How are the barbiturates metabolized?

### **Benzodiazepines:**

(1) Why are benzodiazepines relatively safe? Why are they used?

(2) What is the basic SAR?

(3) Learn some of the representative structures (chlordiazepoxide, diazepam, alprazolam, lorazepam, midazolam, triazolam, ...). Which ones have long/short duration of action? Which are used as anesthetics?

(4) What are two common non-benzodiazepine drugs that have specific  $\alpha 1$  receptor activity?

(5) What is the basic metabolism of the benzodiazepines?

(6) What are agonists, antagonists and inverse agonists of the benzodiazepine receptor?

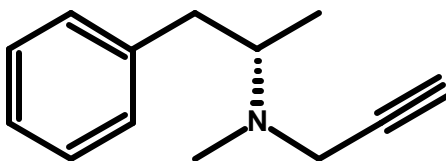
### **Parkinsons**

(1) What is Parkinsons disease and how can we treat it?

(2) Why is dopamine a poor drug for treating Parkinsons?

(3) What are various hypotheses as to the cause of Parkinsons?

(4) Learn about the major drugs used to treat Parkinsons. NOTE: Selegiline was misdrawn in the original notes; the structure has been corrected. What are expected metabolites of Selegiline?



(5) Learn about the pathway from the designer drug MPPP to a toxic metabolite

(6) What are side effects of L-dopa; how can we minimize these?